Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Upon entry of the present amendment, the claims will stand as follows:

Please amend claim 28 as follows:

1. (Previously Presented) A method of diagnosing primary breast cancer in a subject comprising determining the state of methylation of one or more CpG islands in the promoter of RAR β2 nucleic acids isolated from a sample comprising blood, plasma, lymph, duct cells, ductal lavage fluid, nipple aspiration fluid, breast tissue, lymph nodes, bone marrow, or a combination thereof of the subject, wherein a state of hypermethylation of one or more CpG islands in the promoter of RAR β2 nucleic acids as compared with the state of methylation of one or more CpG islands in the promoter of RAR β2 nucleic acids in comparable samples obtained from normal subjects is indicative of primary breast cancer in the subject.

Claims 2-3. (Cancelled)

4. (Original) The method of claim 1, wherein the state of methylation of the nucleic acids is determined simultaneously.

Claims 5-8. (Cancelled)

9. (Previously Presented) The method of claim 1, wherein the sample comprises duct cells obtained by a procedure selected from ductal lavage, sentinel node biopsy, fine needle aspirate, routine operative breast endoscopy, nipple aspiration and core biopsy.

10. (Cancelled)

11. (Previously Presented) The method of claim 1, wherein determining the state of methylation comprises amplifying the nucleic acid by means of at least one sense primer and at least one antisense primer that distinguishes between methylated and unmethylated nucleic acids.

12. (Previously Presented) The method of claim 11, wherein the primers hybridize with target polynucleotide sequences selected from SEQ ID NO:-25-36, 41-48, , and combinations thereof.

13. (Previously Presented) The method of claim 11, wherein the primers are selected from SEQ ID NO:21-24, 37-40, and combinations thereof.

14. (Previously Presented) The method of claim 1, further comprising contacting the nucleic acid with a methylation-sensitive restriction endonuclease.

15. (Original) The method of claim 14, wherein the methylation-sensitive restriction endonuclease is selected from the group consisting of MspI, HpaII, BssHII, BstUI and NotI.

16. (Previously Presented) A method of determining a predisposition to primary breast cancer in a subject comprising determining the state of methylation of one or more CpG islands in the promoter of RARβ2 nucleic acids isolated from a sample comprising blood, plasma, duct cells lymph, ductal lavage fluid, nipple aspiration fluid, breast tissue, lymph nodes bone marrow, or a combination thereof of the subject,

wherein a state of hypermethylation of the CpG islands in the promoter of RAR β2 nucleic acid(s) as compared with the state of methylation of comparable nucleic acid obtained from normal subjects is indicative of a predisposition to primary breast cancer in the subject.

Claims 17-19. (Cancelled)

20. (Previously Presented) The method of claim 16, wherein the sample comprises duct cells obtained by a procedure selected from the group consisting of ductal lavage, sentinel node biopsy, fine needle aspirate, routine operative breast endoscopy, nipple aspiration and core biopsy.

21. (Cancelled)

22. (Original) The method of claim 16, wherein determining the state of methylation comprises amplifying the nucleic acid(s) by means of at least one sense primer and at least one antisense primer that distinguishes between methylated and unmethylated nucleic acid.

23. (Original) The method of claim 22, wherein the nucleic acids are amplified simultaneously.

24. (Previously Presented) The method of claim 22, wherein the primers hybridize with target polynucleotide sequences selected from SEQ ID NO:25-36, 41-48, and combinations thereof.

25. (Previously Presented) The method of claim 24, wherein the primers are selected from SEQ ID NO:21-24, 37-40, and combinations thereof.

26. (Original) The method of claim 16, further comprising contacting the nucleic acid with a methylation-sensitive restriction endonuclease.

27. (Original) The method of claim 26, wherein the methylation-sensitive restriction endonuclease is selected from the group consisting of MspI, HpaII, BssHII, BstUI and NotI.

28. (Currently Amended) A method for [diagnosing] detecting primary breast cancer in a subject comprising:

(a) contacting a nucleic acid-containing specimen selected from blood, plasma, lymph, duct cells, ductal lavage fluid, nipple aspiration fluid, breast tissue, lymph nodes bone marrow, or a combination thereof, of the subject with an agent that provides a determination of the methylation state of CpG islands in the promoter of RARβ2 nucleic acids in the specimen, and

(b) identifying the methylation state of at least one CpG island in the promoter of RARβ2, wherein the CpG islands in the promoter of RARβ2 is hypermethylated compared to the methylation state of ~~the same region of the same nucleic acid in~~ CpG islands in comparable samples obtained from normal subjects.

Claims 29-33. (Cancelled)

34. (Previously Presented) The method of claim 28, wherein the agent is at least one sense primer and at least one antisense primer that hybridize with a target sequence in the nucleic acid.

35. (Previously Presented) The method of claim 34, wherein the primers hybridize with target polynucleotide sequences selected from SEQ ID NO:25-36, 41-48, and combinations thereof.

36. (Previously Presented) The method of claim 34, wherein the primers are selected from SEQ ID NO:21-24, 37-40, and combinations thereof.

Claims 37-39. (Cancelled)

40. (Previously Presented) The method of claim 34, wherein the method employs multiplex methylation-specific PCR.

41. (Original) The method of claim 40, wherein the specimen comprises breast duct or ductal fluid.

Claims 42-44. (Cancelled)